CONTRACT CONCEPT REVIEW

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Concept Title: **Laboratory Studies for the National Toxicology Program to Evaluate Toxicity following Early Life Exposure to Chemicals**

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I. Objective

The overall objective of this contract is to facilitate NTP's efforts to characterize the potential adverse effects of chemical, physical, or biological agents when administration begins during early life-stages that are critical periods of development. Objectives will include investigations on: (1) fertility and reproductive performance, and (2) pre- and post-natal developmental effects, including effects that might occur during adulthood following *in utero* and perinatal exposures.

The scope of the required activities is too great, and the space and personnel needed to conduct these studies exceeds that available at the NIEHS; therefore, studies are to be carried out through contract mechanisms.

II. Background

The NTP has actively investigated adverse reproductive and developmental effects of chemicals in rodents as part of its broad mandate to characterize the toxicity of agents of public health concern. These research and testing activities are fundamental to addressing specific deficiencies in the toxicology database for many chemicals as well as to explore new approaches to toxicology testing within the program. Studies to investigate adverse reproductive and developmental effects are usually conducted in non-government facilities in accordance with Good Laboratory Practices.

Childhood environmental exposures, childhood cancers, and developmental disabilities are all key areas of public health concern. In addition, children may be more vulnerable to some environmental exposures than adults. Thus, the NTP plans a series of testing and research activities aimed at expanding the current boundaries around reproductive toxicity testing to include *in utero* development, postnatal development, and specialized assessments following subsequent longer term exposure. These evaluations will allow for the study of a broad range of childhood specific toxicities and enable the determination of whether such toxicities will have long-term consequences that span into adulthood.

The envisioned studies will require flexible designs as it is not anticipated that the studies will be mere standardized testing protocols. The ability to conduct the following endpoint assessments defines some of the scope of the this research program:

- generation of dose-response information from short term as well as long term repeated exposures,
- exposure via multiple pathways (*e.g.*, *in utero,* lactational, oral),
- assessments of maternal and fetal toxicity,
- gestational and lactational indices of toxicity,
- pre- and postnatal developmental evaluations (such as neurotoxicity),
- assessments of sexual development, estrus cyclicity, spermatogenesis, clinical pathology, tissue histopathology, and
- evaluation of reproductive capabilities across generations.

III. Priority

The studies conducted under these contracts are of high priority because they constitute the NTP's core research and testing efforts to carry out toxicology studies designed to evaluate developmental, reproductive and longer term testing in rodents. While alternative approaches are under development and evaluation, these current efforts are recognized internationally as established and accepted approaches for evaluating the impact of environmental agents in rodent models as a means for identifying potential health hazards for humans.

These research and testing activities will help NTP achieve its goals of testing agents of public health concern, strengthening the science base in toxicology, and providing information to health regulatory and research agencies, scientific and medical communities, and the public. Governmental and non-government groups worldwide recognize the findings from NTP studies as authoritative, and reports from these studies will be publicly available.